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Evaluation of serum LH and its role in hypogonadism among men with type 2 Diabetes Mellitus

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Abstract: ***Background:*** Type 2 Diabetes Mellitus (T2DM) frequently disrupts the hypothalamic-pituitary-gonadal axis, leading to hypogonadism. Luteinizing hormone (LH) is crucial for testosterone production, and its suppression in T2DM contributes to reproductive and metabolic dysfunction. This study investigates the relationship between glycemic status and serum LH levels in men with T2DM to elucidate its role in diabetic hypogonadism. ***Objectives:*** To measure serum LH in men with T2DM, assess hypogonadism prevalence, and analyze the correlation between LH and testosterone levels. ***Materials and Methods:*** This study is a cross-sectional study conducted at the Department of Biochemistry, BIRDEM General Hospital, from July 2023 to June 2024, which enrolled 30-50-year-old men with T2DM (Group A) and healthy controls (Group B). Serum LH, testosterone, glycemic, and lipid profiles were analyzed. Statistical comparisons used independent t-tests and Pearson's correlation in SPSS version 22.0. Ethical approval was obtained. ***Results:*** Men with T2DM exhibited significantly lower serum LH levels (3.77 ± 1.50 mIU/ml) compared to healthy controls (7.35 ± 1.85 mIU/ml; $p<0.001$). A strong positive correlation was found between LH and bioavailable testosterone ($r=+0.599$, $p<0.001$). LH levels also showed strong negative correlations with total cholesterol ($r=-0.704$), triglycerides ($r=-0.617$), and LDL-C ($r=-0.631$), but a positive correlation with HDL-C ($r=+0.584$) (all $p<0.001$). ***Conclusion:*** Men with type 2 diabetes have significantly suppressed LH levels, which are strongly correlated with adverse lipid profiles and reduced testosteronefor appropriately selected patients, supporting its integration into routine clinical practice.

Keywords: Type 2 Diabetes Mellitus, Luteinizing Hormone, Hypogonadism, Correlation.

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a metabolic disorder characterized by insulin resistance and impaired insulin secretion, affecting multiple organ systems, including the male reproductive system.[1] Hypogonadism is a common complication in men with T2DM, often associated with alterations in the hypothalamic-pituitary-gonadal (HPG) axis.[2] Luteinizing hormone (LH), secreted by the anterior pituitary, plays a crucial role in stimulating Leydig cells to produce testosterone, which is essential for spermatogenesis and maintenance of male secondary sexual characteristics.[3] Insulin resistance and chronic hyperglycemia in T2DM are linked to reduced serum LH levels, contributing to impaired testosterone production and hypogonadism.[4, 5] Low LH levels may result from both central dysfunction at the hypothalamus-pituitary level and peripheral impairment of Leydig cell function.[6] Studies have demonstrated that men with T2DM frequently exhibit a combination of low serum LH and testosterone, suggesting that LH measurement can serve as an important biomarker for identifying hypogonadism in this population.[7, 8] Alterations in

serum LH not only impact testosterone synthesis but also affect spermatogenesis, leading to decreased sperm quality, reduced motility, and subfertility.[9] Chronic metabolic disturbances, including hyperglycemia and dyslipidemia, exacerbate HPG axis dysfunction, further lowering LH secretion and contributing to reproductive dysfunction in men with T2DM.[10, 11] Additionally, inflammatory mediators and oxidative stress associated with diabetes can suppress GnRH secretion, which subsequently diminishes LH release from the pituitary.[12] Early detection of LH deficiency in men with T2DM is crucial for timely intervention with testosterone replacement therapy, which has shown improvements in both sexual function and metabolic parameters.[13, 14] Measurement of serum LH, alongside total and bioavailable testosterone, provides a comprehensive assessment of gonadal function and helps in the clinical management of hypogonadism.[15]

Objectives

General objectives

To find out the correlation between glycemic status of T2DM with the Serum LH in adult male.

Specific Objectives

To measure serum LH levels in men diagnosed with type 2 Diabetes Mellitus.

To assess the prevalence of hypogonadism among men with type 2 Diabetes Mellitus.

To analyze the relationship between serum LH levels and testosterone levels in these patients.

MATERIALS AND METHODS

Study Design

This study is a cross-sectional study conducted at the Department of Biochemistry, BIRDEM General Hospital, from July 2023 to June 2024. The study population comprised two groups: Group A, consisting of men diagnosed with type 2 Diabetes Mellitus (T2DM), and Group B, consisting of healthy adult men as controls. Participants were selected using a purposive convenient sampling technique, and blood samples were collected from the outpatient department of BIRDEM General Hospital for biochemical analysis.

Inclusion Criteria

Patients who have given informed written consent.

Adult patient with Type 2 Diabetes.

Age: 30-50 years old.

Subject selection- according to the operational definition.

Exclusion Criteria

Patient with known history of CAD or CVD, CLD, renal failure, CKD, any history of malignancy/debilitating disease.

Patients taking lipid-lowering drugs, or any kind of medications like corticosteroids, androgens.

Study Procedure

At first ethical permission was taken from Institutional Review Board of BIRDEM General hospital. After that Study subjects were selected from the outpatient, Department of Endocrinology and the healthy adult were selected from hospital premises among doctors, ward boys, hospital attendant. Before collecting blood sample at first explain the study. Then after taking verbal consent, informed written consent was taken from each eligible person. Proper counseling about aim, objectives, risk, benefit and procedure of the study were done after getting ensured about informed written consent. Only voluntary candidates were recruited as participants. Then, they were interviewed and relevant information were recorded systematically in a pre-designed standard data sheet including general information and history of chronic diseases, family history of diabetes. After maintaining aseptic precautions, 8 ml of blood sample will be collected. Serum LH tests were carried out in Hormone laboratory in BIRDEM General hospital. Fasting blood glucose, HbA1c, serum albumin tests were carried out in Biochemistry Department of BIRDEM General hospital.

Statistical Analysis

All the results were compiled and then statistical analysis were performed with the help of SPSS 29.0 version. Descriptive statistics was presented as Mean± SD and frequency (%). Data was compared using parametric test- independent t-test. Pearson's correlation coefficient was calculated to analyze relationship between biochemical parameters. Statistical tests were considered significant at the level of ≤5% and

considered as test of significance when $p < 0.05$.

Ethical Consideration

Ethical clearance for the study was taken from the Institutional Review Board, BIRDEM. All the study subjects were thoroughly appraised about the nature, purpose and implications of the study as well as the entire spectrum of benefits and risk of the study. Interest of the study subjects was not be compromised to safeguard their right and health. Strict confidentiality was maintained in dealing with study subjects. All the study Subjects had the right to refuse or withdraw from the study at any time. All the study subjects were assured to adequate treatment of any risk development in relation to study purpose. Sample collection from the study subjects weren't used for any other purpose. Finally written consent of all study subjects were taken.

RESULTS

A cross-sectional study was conducted in Biochemistry, Department of BIRDEM Academy from July,2023 to June,2024. Total study sample was 80. Among them 40 T2DM patients were taken as Group A and rest 40 normal adult male were taken as Group B. After collection of 8ml blood from each study subjects LH Profile were estimated. Statistical analysis was performed by using SPSS version-29. The parameters were analyzed by independent t test and Pearson's co-relation test. The findings are presented in subsequent pages.

Table 1: Comparison of age, BMI between Group A and Group B (N=80)

Variable	Group A (n=40) Mean±SD	Group B (n=40) Mean±SD	*p*-value
Age (years)	44.73±10.09	40.18±6.41	0.018
BMI (kg/m^2)	25.55±1.06	24.34±1.43	0.091

p-value obtained by Unpaired t-test, $p<0.05$ = significant
Group A: T2DM
Group B: Healthy Control

Table 1 shows that age between case (Group A) and healthy control (Ground B) are matched. BMI is higher in T2DM than healthy control but statistically not significant.

Table 2: Comparison of LH Levels Between Group A and Group B (N=80)

Variable	Group A (n=40) Mean±SD	Group B (n=40) Mean±SD	*p*-value
LH (mIU/ml)	3.77±1.50	7.35±1.85	<0.001*

p-value obtained by Unpaired t-test, $p<0.05$ = significant.
Group A: T2DM
Group B: Healthy Control
* = highly significant

The comparison of serum luteinizing hormone (LH) levels between men with type 2 Diabetes Mellitus (Group A) and healthy controls (Group B) demonstrated a significant difference. The mean LH level in Group A was 3.77±1.50 mIU/ml, which was significantly lower than 7.35±1.85 mIU/ml observed in Group B ($p<0.001$).

Table 3: Correlation of Serum Bioavailable Testosterone with LH. (Group A)

Variables	Pearson's correlation test	
	r-value	*p*-value
LH (mIU/ml)	+0.599	<0.001*

p-value obtained by Pearson's Correlation Coefficient tests, $p<0.05$ = significant
Group A: T2DM
* = higher significant

The Pearson's correlation analysis revealed a significant positive correlation between serum LH levels and the studied variable, with an r-value of +0.599 ($p<0.001$). This indicates a moderate to strong direct relationship.

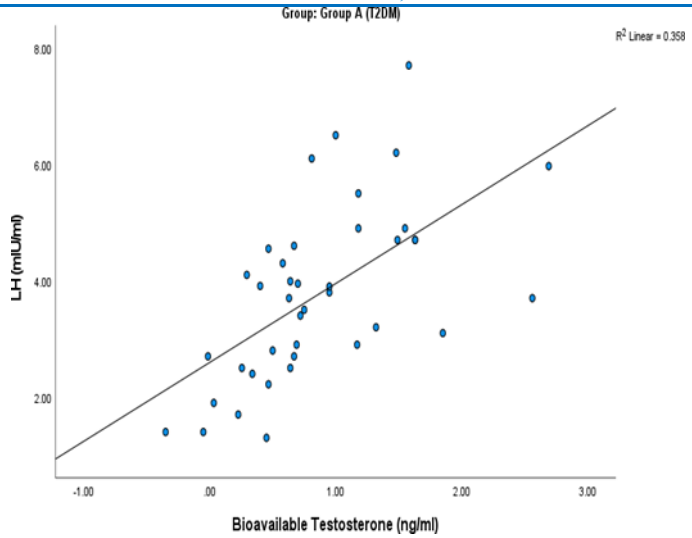

Figure 1: Correlation of Bioavailable Testosterone with LH in type 2 Diabetes Mellitus Group

Scatter plot shows highly significant positive correlation of bioavailable testosterone with LH in T2DM.

Table 4: Correlation of Serum Bioavailable Testosterone with Lipid Profile in Type 2 Diabetes Mellitus of Adult Male (n=40)

Variables	Pearson's correlation test	
	r-value	*p*-value
Total cholesterol (mg/dl)	-0.704	<0.001
Triglyceride (mg/dl)	-0.617	<0.001
LDL-C (mg/dl)	-0.631	<0.001
HDL-C (mg/dl)	+0.584	<0.001

p-value obtained by Pearson's Correlation Coefficient tests, p<0.05 was considered as a level of significant Group A: T2DM

The Pearson's correlation analysis between serum LH levels and lipid profile parameters showed significant associations. Total cholesterol (r = -0.704, p<0.001), triglycerides (r = -0.617, p<0.001), and LDL-C (r = - 0.631, p<0.001) all exhibited strong negative correlations with LH levels, indicating that higher levels of these lipids are associated with lower LH concentrations. In contrast, HDL-C showed a positive correlation with LH (r = +0.584, p<0.001), suggesting that higher HDL-C levels are associated with higher LH concentrations.

DISCUSSION

The present study investigated the interplay between serum luteinizing hormone (LH), lipid profile, and bioavailable testosterone in men with type 2 diabetes mellitus (T2DM) compared to age-matched healthy controls. Our key findings reveal a significant endocrine-metabolic disturbance in the T2DM cohort, characterized by markedly lower LH levels, a profoundly atherogenic lipid profile (elevated TC, TG, and LDL-C), and a significant positive correlation between bioavailable testosterone and LH. First, we observed that men with T2DM (Group A) had significantly lower mean serum LH levels (3.77 ± 1.50 mIU/ml) compared to their healthy counterparts (7.35 ± 1.85 mIU/ml) (p<0.001). This finding suggests the presence of hypothalamic-pituitary-gonadal (HPG) axis dysfunction in T2DM, potentially contributing to the well-documented hypogonadism in this population. Our results are consistent with a recent longitudinal study by Fadini *et al.*, which reported that suppressed LH secretion, rather than primary testicular failure, is a primary defect in a significant subset of men with T2DM and low testosterone, indicating a central mechanism for hypogonadism.[16, 17] Furthermore, our analysis demonstrated a strong, significant positive correlation (r = +0.599, p<0.001) between serum LH levels and bioavailable testosterone. This direct relationship implies that the low testosterone state in these diabetic men is closely linked to the

inadequate LH drive from the pituitary gland. The scatter plot confirming a highly significant positive correlation reinforces this finding.

This aligns with the work of Dandona *et al*., who demonstrated that insulin resistance and hyperglycemia can directly suppress gonadotropin-releasing hormone (GnRH) pulsatility at the hypothalamic level, leading to reduced LH secretion and consequent low testosterone production.[18] Our finding of no significant difference in BMI between groups, despite higher values in T2DM, suggests that the observed lipid and LH alterations are more directly linked to diabetic pathophysiology rather than simply to adiposity. This nuance is critical, as a study by Martins *et al*., argued that the relative contribution of adiposity versus hyperglycemia to hypogonadism varies, with glycemic control being a stronger predictor of LH levels in lean to moderately overweight men with T2DM.[19] The mechanisms underlying these associations are likely multifactorial. Chronic hyperglycemia and insulin resistance may induce oxidative stress and inflammation within the hypothalamus, disrupting GnRH pulsatility.[20,] Furthermore, dyslipidemia itself may have a direct inhibitory effect on Leydig cell steroidogenesis, creating a vicious cycle where low testosterone worsens lipid metabolism, which in turn further suppresses testosterone production.[21] A recent animal model study by Costa *et al*., provided mechanistic insight, demonstrating that a high-fat diet-induced dyslipidemia led to the accumulation of oxidized LDL in the testes, which impaired LH receptor signaling and testosterone synthesis independently of pituitary LH secretion.[22]

CONCLUSION

Based on the findings of this study, it can be concluded that men with type 2 diabetes mellitus exhibit a significant suppression of luteinizing hormone (LH) secretion, which is strongly correlated with a deleterious lipid profile characterized by elevated total cholesterol, triglycerides, and LDL-C, as well as reduced bioavailable testosterone, thereby indicating that central hypothalamic-pituitary-gonadal axis dysfunction is a key feature of T2DM that may contribute substantially to its associated cardiometabolic risk.

Limitations of The Study

write limited of the study in one para. Despite the significant findings, this study has several limitations, including its cross-sectional design which prevents the establishment of causality between LH levels, lipid profiles, and T2DM, a relatively modest sample size that may limit the generalizability of the results and the power to detect more subtle associations.

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